

LISTING OF THE CLAIMS

Claim 1 (**currently amended**) A method for the production of a single heavy chain antibody in a non-human mammal comprising the step of expressing a heterologous VHH heavy chain locus in that mammal specifically in B cells in response to antigen challenge, wherein the VHH heavy chain locus comprises:

(a) ~~at least one VHH region each comprising one VHH exon, at least one D region each comprising one D exon and at least one J region each comprising one J exon,~~ wherein the VHH exon region, the D exon region and the J exon region are capable of recombining to form VDJ coding sequence,

(b) a constant heavy chain region comprising at least one C μ constant heavy chain gene and at least one of C γ , C α , C ϵ , or C δ constant heavy chain gene, wherein each of said constant heavy chain genes, when expressed, does not express a functional CH1 domain,

(c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells and

~~which locus when expressed leads to the formation of a single heavy chain antibody~~
said method comprising:

1) immunizing said mammal with an antigen and

2) isolating single heavy chain antibody against said antigen from said mammal.

Claim 2 (**canceled**)

Claim 3 (**currently amended**) A method for the production of a single heavy chain antibody in a non-human mammal comprising the step of expressing a camelised VH heavy chain locus in that mammal specifically in B cells in response to antigen challenge, wherein the

camelised VH heavy chain locus comprises:

(a) at least one ~~VH region each comprising one~~ VH exon which is mutated such that, when expressed, the resulting single heavy chain antibody is stabilised, at least one ~~D region each comprising one~~ D exon and at least one ~~J region comprising one~~ J exon, wherein the VH exon region, the D exon region and the J exon region are capable of recombining to form VDJ coding sequence, and

(b) a constant heavy chain region comprising at least one C μ constant heavy chain gene and at least one of C γ , C α , C ϵ , or C δ constant heavy chain gene, wherein each of said constant heavy chain genes, when expressed, does not express a functional CH1 domain,

(c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells and

~~which locus when expressed leads to the formation of a single heavy chain antibody~~
said method comprising:

1) immunizing said mammal with an antigen and

2) isolating single heavy chain antibody against said antigen from said mammal.

Claims 4 – 6 (canceled)

Claim 7 (currently amended) A method according to claim 1 wherein the VHH single heavy chain locus comprises a camelid VHH, at least one D exon region of human origin and at least one J exon region of human origin and a constant region of human origin.

Claim 8 (currently amended) A method according to claim 3 wherein the camelised VH heavy chain locus comprises at least one D exon region of human origin and at least one J exon region of human origin and a constant region of human origin.

Claim 9 (canceled)

Claim 10 (currently amended) A method according to claim 1 or 3 wherein the constant heavy chain region comprises at least one constant region heavy chain gene which is of non-camelid origin.

Claim 11 (original) A method according to claim 10 wherein at least one constant region heavy chain gene is of human origin.

Claims 12 – 16 (canceled)

Claims 17 -32 (canceled)

Claim 33 (previously presented) The method of claim 1 wherein the entire VHH single heavy chain locus is of camelid origin

Claim 34 (previously presented) The method of claim 3 wherein the camelised VH single heavy chain locus is of human origin.

Claim 35 (previously presented) The method of claim 3 wherein the camelised VH single heavy chain locus is of non-human origin.

Claim 36 (previously presented) The method of claim 3 wherein the camelised VH single heavy chain locus is of camelid origin.

Claims 37 -38 (canceled)

Claim 39 (new) The method according to claim 1 or 3 wherein the non-human mammal is a rodent.

Claim 40 (new) The method according to claim 1 or 3 wherein the regulatory sequence is a locus control region.